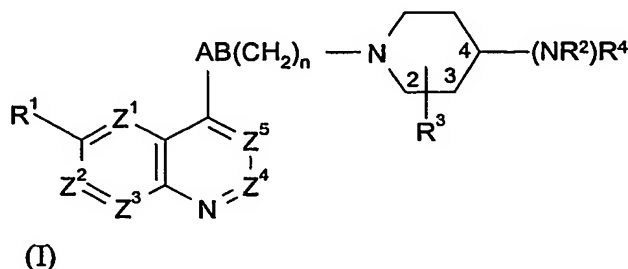


Claims

1. a compound of formula (I) or a pharmaceutically acceptable derivative thereof:



wherein:

one of Z^1 , Z^2 , Z^3 , Z^4 and Z^5 is N, one is CR^{1a} and the remainder are CH, or one or two of Z^1 , Z^2 , Z^3 , Z^4 and Z^5 are independently CR^{1a} and the remainder are CH;

R^1 and R^{1a} are independently hydrogen; hydroxy; (C_{1-6}) alkoxy optionally substituted by (C_{1-6}) alkoxy, amino, piperidyl, guanidino or amidino any of which is optionally N-substituted by one or two (C_{1-6}) alkyl, acyl or (C_{1-6}) alkylsulphonyl groups, $CONH_2$, hydroxy, (C_{1-6}) alkylthio, heterocyclylthio, heterocyclioxy, arylthio, aryloxy, acylthio, acyloxy or (C_{1-6}) alkylsulphonyloxy; (C_{1-6}) alkoxy-substituted (C_{1-6}) alkyl; halogen; (C_{1-6}) alkyl; (C_{1-6}) alkylthio; trifluoromethyl; trifluoromethoxy; nitro; azido; acyl; acyloxy; acylthio; (C_{1-6}) alkylsulphonyl; (C_{1-6}) alkylsulphoxide; arylsulphonyl; arylsulphoxide or an amino, piperidyl, guanidino or amidino group optionally N-substituted by one or two (C_{1-6}) alkyl, acyl or (C_{1-6}) alkylsulphonyl groups;

or when Z^5 is CR^{1a} , R^{1a} may instead be cyano, hydroxymethyl or carboxy;

or R^1 and R^{1a} on adjacent positions may together form ethylenedioxy;

provided that when Z^1 , Z^2 , Z^3 , Z^4 and Z^5 are CR^{1a} or CH, then R^1 is not hydrogen;

R^2 is hydrogen, or (C_{1-4}) alkyl or (C_{2-4}) alkenyl optionally substituted with 1 to 3 groups selected from:

amino optionally substituted by one or two (C_{1-4}) alkyl groups; carboxy; (C_{1-4}) alkoxycarbonyl; (C_{1-4}) alkylcarbonyl; (C_{2-4}) alkenyloxycarbonyl; (C_{2-4}) alkenylcarbonyl; aminocarbonyl wherein the amino group is optionally substituted by hydroxy, (C_{1-4}) alkyl, hydroxy (C_{1-4}) alkyl, aminocarbonyl (C_{1-4}) alkyl, (C_{2-4}) alkenyl, (C_{1-4}) alkylsulphonyl, trifluoromethylsulphonyl, (C_{2-4}) alkenylsulphonyl, (C_{1-4})

4)alkoxycarbonyl, (C₁₋₄)alkylcarbonyl, (C₂₋₄)alkenyloxycarbonyl or (C₂₋₄)alkenylcarbonyl; cyano; tetrazolyl; 2-oxo-oxazolidinyl optionally substituted by R¹⁰; 3-hydroxy-3-cyclobutene-1,2-dione-4-yl; 2,4-thiazolidinedione-5-yl; tetrazol-5-ylaminocarbonyl; 1,2,4-triazol-5-yl optionally substituted by R¹⁰; 5-oxo-1,2,4-oxadiazol-3-yl; halogen; (C₁₋₄)alkylthio; trifluoromethyl; hydroxy optionally substituted by (C₁₋₄)alkyl, (C₂₋₄)alkenyl, (C₁₋₄)alkoxycarbonyl, (C₁₋₄)alkylcarbonyl, (C₂₋₄)alkenyloxycarbonyl, (C₂₋₄)alkenylcarbonyl; oxo; (C₁₋₄)alkylsulphonyl; (C₂₋₄)alkenylsulphonyl; or (C₁₋₄)aminosulphonyl wherein the amino group is optionally substituted by (C₁₋₄)alkyl or (C₂₋₄)alkenyl;

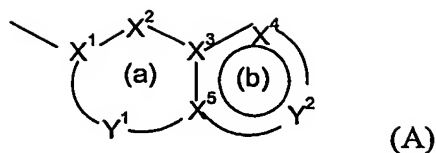
R³ is in the 2-, 3- or 4-position and is trifluoromethyl or is in the 2-position and is oxo; or R³ is in the 3-position and is fluorine or amino wherein the amino group is optionally substituted by: hydroxy; (C₁₋₆)alkylsulphonyl; trifluoromethylsulphonyl; (C₂₋₆)alkenylsulphonyl; (C₁₋₆)alkylcarbonyl; (C₂₋₆)alkenylcarbonyl; (C₁₋₆)alkoxycarbonyl; (C₂₋₆)alkenyloxycarbonyl; (C₁₋₆)alkyl; or (C₂₋₆)alkenyl; wherein a (C₁₋₆)alkyl or (C₂₋₆)alkenyl moiety may be optionally substituted with up to 2 groups R¹² independently selected from:

halogen; (C₁₋₆)alkylthio; trifluoromethyl; cyano; carboxy; tetrazolyl; 2-oxo-oxazolidinyl; 3-hydroxy-3-cyclobutene-1,2-dione-4-yl; 2,4-thiazolidinedione-5-yl; tetrazol-5-ylaminocarbonyl; 1,2,4-triazol-5-yl optionally substituted by R¹⁰; or 5-oxo-1,2,4-oxadiazol-3-yl; (C₁₋₆)alkoxycarbonyl; (C₁₋₆)alkylcarbonyl; (C₂₋₆)alkenyloxycarbonyl; (C₂₋₆)alkenylcarbonyl; hydroxy optionally substituted by (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₁₋₆)alkylcarbonyl, (C₂₋₆)alkenylcarbonyl or aminocarbonyl wherein the amino group is optionally substituted by (C₁₋₆)alkyl, (C₂₋₆)alkenyl; amino optionally mono- or disubstituted by (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, (C₂₋₆)alkenyloxycarbonyl, (C₂₋₆)alkenylcarbonyl, (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₁₋₆)alkylsulphonyl, (C₂₋₆)alkenylsulphonyl or aminocarbonyl wherein the amino group is optionally substituted by (C₁₋₆)alkyl or (C₂₋₆)alkenyl; in addition when R³ is disubstituted with a hydroxy or amino containing substituent and carboxy containing substituent these may together form a cyclic ester or amide linkage, respectively;

R⁴ is a group -U-R⁵ where

U is selected from CO, SO₂ and CH₂ and

R⁵ is an optionally substituted bicyclic carbocyclic or heterocyclic ring system (A):



containing up to four heteroatoms in each ring in which

ring (a) is aromatic or non aromatic;

X^1 is C when part of an aromatic ring or CR^{14} when part of a non aromatic ring;

X^2 is N, NR^{13} , O, $S(O)_x$, CO or CR^{14} when part of an aromatic or non-aromatic ring or may in addition be $CR^{14}R^{15}$ when part of a non aromatic ring;

X^4 is N, NR^{13} , O, $S(O)_x$, CO or CR^{14} ;

X^3 and X^5 are independently N or C;

Y^1 is a 1 to 3 atom linker group each atom of which is independently selected from N, NR^{13} , O, $S(O)_x$, CO and CR^{14} when part of an aromatic or non-aromatic ring or may additionally be $CR^{14}R^{15}$ when part of a non aromatic ring,

Y^2 is a 2 or 3 atom linker group completing an aromatic ring, each atom of Y^2 being independently selected from N, NR^{13} , O, $S(O)_x$, CO and CR^{14} ;

each of R^{14} and R^{15} is independently selected from: H; (C_{1-4}) alkylthio; halo; carboxy (C_{1-4}) alkyl; halo (C_{1-4}) alkoxy; halo (C_{1-4}) alkyl; (C_{1-4}) alkyl; (C_{2-4}) alkenyl; (C_{1-4}) alkoxycarbonyl; formyl; (C_{1-4}) alkylcarbonyl; (C_{2-4}) alkenyloxycarbonyl; (C_{2-4}) alkenylcarbonyl; (C_{1-4}) alkylcarbonyloxy; (C_{1-4}) alkoxycarbonyl (C_{1-4}) alkyl; hydroxy; hydroxy (C_{1-4}) alkyl; mercapto (C_{1-4}) alkyl; (C_{1-4}) alkoxy; nitro; cyano; carboxy; amino or aminocarbonyl optionally substituted as for corresponding substituents in R^3 ; (C_{1-4}) alkylsulphonyl; (C_{2-4}) alkenylsulphonyl; or aminosulphonyl wherein the amino group is optionally mono- or di-substituted by (C_{1-4}) alkyl or (C_{2-4}) alkenyl; aryl; aryl (C_{1-4}) alkyl; aryl (C_{1-4}) alkoxy or

R^{14} and R^{15} may together represent oxo;

each R^{13} is independently H; trifluoromethyl; (C_{1-4}) alkyl optionally substituted by hydroxy, (C_{1-6}) alkoxy, (C_{1-6}) alkylthio, carboxy, halo or trifluoromethyl; (C_{2-4}) alkenyl; aryl; aryl (C_{1-4}) alkyl; arylcarbonyl; heteroarylcarbonyl; (C_{1-4}) alkoxycarbonyl; (C_{1-4}) alkylcarbonyl; formyl; (C_{1-6}) alkylsulphonyl; or aminocarbonyl wherein the amino group is optionally substituted by (C_{1-4}) alkoxycarbonyl, (C_{1-4}) alkylcarbonyl, (C_{2-4}) alkenyloxycarbonyl, (C_{2-4}) alkenylcarbonyl, (C_{1-4}) alkyl or (C_{2-4}) alkenyl and optionally further substituted by (C_{1-4}) alkyl or (C_{2-4}) alkenyl;

n is 0 or 1;

each x is independently 0, 1 or 2

A is NR^{11} , O or CR^6R^7 and B is NR^{11} , O, SO_2 or CR^8R^9 and wherein:
 each of R^6 , R^7 , R^8 and R^9 is independently selected from: hydrogen; (C₁₋₆)alkoxy; (C₁₋₆)alkylthio; halo; trifluoromethyl; azido; (C₁₋₆)alkyl; (C₂₋₆)alkenyl; (C₁₋₆)alkoxycarbonyl; (C₁₋₆)alkylcarbonyl; (C₂₋₆)alkenyloxycarbonyl; (C₂₋₆)alkenylcarbonyl; hydroxy, amino or aminocarbonyl optionally substituted as for corresponding substituents in R^3 ; (C₁₋₆)alkylsulphonyl; (C₂₋₆)alkenylsulphonyl; or aminosulphonyl wherein the amino group is optionally substituted by (C₁₋₆)alkyl or (C₂₋₆)alkenyl;
 or when $n=1$ R^6 and R^8 together represent a bond and R^7 and R^9 are as above defined;
 or R^6 and R^7 or R^8 and R^9 together represent oxo;

provided that:

when A is NR^{11} , B is not NR^{11} or O;

when A is CO, B is not CO, O or SO_2 ;

when n is 0 and A is NR^{11} , CR^8R^9 can only be CO;

when A is CR^6R^7 and B is SO_2 , n is 0;

when n is 0, B is not NR^{11} or O or R^8 and R^9 are not optionally substituted hydroxy or amino;

when A is O, B is not NR^{11} , O, SO_2 or CO and $n=1$; and

when A-B is $\text{CR}^7=\text{CR}^9$, n is 1

R^{10} is selected from (C₁₋₄)alkyl; (C₂₋₄)alkenyl and aryl any of which may be optionally substituted by a group R^{12} as defined above; carboxy; aminocarbonyl wherein the amino group is optionally substituted by hydroxy, (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₁₋₆)alkylsulphonyl, trifluoromethylsulphonyl, (C₂₋₆)alkenylsulphonyl, (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, (C₂₋₆)alkenyloxycarbonyl or (C₂₋₆)alkenylcarbonyl and optionally further substituted by (C₁₋₆)alkyl or (C₂₋₆)alkenyl; (C₁₋₆)alkylsulphonyl; trifluoromethylsulphonyl; (C₂₋₆)alkenylsulphonyl; (C₁₋₆)alkoxycarbonyl; (C₁₋₆)alkylcarbonyl; (C₂₋₆)alkenyloxycarbonyl; and (C₂₋₆)alkenylcarbonyl; and

R^{11} is hydrogen; trifluoromethyl, (C₁₋₆)alkyl; (C₂₋₆)alkenyl; (C₁₋₆)alkoxycarbonyl; (C₁₋₆)alkylcarbonyl; or aminocarbonyl wherein the amino group is optionally substituted by (C₁₋₆)alkoxycarbonyl, (C₁₋₆)alkylcarbonyl, (C₂₋₆)alkenyloxycarbonyl, (C₂₋₆)alkenylcarbonyl, (C₁₋₆)alkyl or (C₂₋₆)alkenyl and optionally further substituted by (C₁₋₆)alkyl or (C₂₋₆)alkenyl;

or where one of R³ and R⁶, R⁷, R⁸ or R⁹ contains a carboxy group and the other contains a hydroxy or amino group they may together form a cyclic ester or amide linkage.

2. A compound according to claim 1 wherein Z⁵ is CH, C-Cl or N, Z³ is CH or CF and Z¹, Z² and Z⁴ are each CH, or Z¹ is N, Z³ is CH and Z² and Z⁴ are each CH and Z⁵ is CH or C-Cl.

3. A compound according to any preceding claim wherein R¹ is methoxy and R^{1a} is H or when Z³ is CR^{1a} it may be C-F or when Z⁵ is CR^{1a} it may be C-F or C-Cl.

4. A compound according to any preceding claim wherein R² is hydrogen, carboxymethyl, hydroxyethyl, aminocarbonylmethyl, ethoxycarbonylmethyl, ethoxycarbonylallyl or carboxyallyl.

5. A compound according to any preceding claim wherein R³ is CF₃, fluoro, oxo or amino unsubstituted or substituted by (C₁₋₆)alkyl or (C₂₋₆)alkenyl.

6. A compound according to any preceding claim wherein n is 0, A-B is CHOH-CH₂, NR¹¹-CH₂, NR¹¹-CO or CH₂-CH₂ and R¹¹ is hydrogen or (C₁₋₄)alkyl.

7. A compound according to any preceding claim wherein U is CH₂ and R⁵ is an aromatic heterocyclic ring (A) having 1-4 heteroatoms of which one is N or NR¹³, R¹³ is H if in ring (a) or in addition (C₁₋₄)alkyl if in ring (b), R¹⁴ and R¹⁵ are independently selected from hydrogen, halo, hydroxy, (C₁₋₄)alkyl, (C₁₋₄)alkoxy, trifluoromethoxy, nitro, cyano, aryl(C₁₋₄)alkoxy and (C₁₋₄)alkylsulphonyl.

8. A compound according to any of claims 1 to 6 wherein R⁵ is 4,6-difluoro-indol-2-yl, 1H-pyrrolo[2,3-b]-pyridin-2-yl, 1H-pyrrolo[3,2-b]-pyridin-2-yl, 8-hydroxy-quinolin-2-yl, quinoxalin-2-yl, benzimidazol-2-yl, benzo[1,2,3]-thiadiazol-5-yl, benzothiophen-2-yl, 4,6-difluoro-1H-benzimidazol-2-yl, benzothiazole-5-yl, 3-(R)-2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-3-yl or [1,2,3]thiadiazolo[5,4-b]pyridin-6-yl.

9. A compound according to claim 1 selected from:

6-[(3*S*,4*R*)-3-fluoro-1-[(*R*)-2-hydroxy-2-(6-methoxyquinolin-4-yl)-ethyl]piperidin-4-ylamino)methyl]-[1,2,3]thiadiazolo[5,4-b]pyridine and 6-[(3*R*,4*S*)-3-fluoro-1-[(*R*)-2-hydroxy-2-(6-methoxyquinolin-4-yl)-ethyl]piperidin-4-ylamino)methyl]-[1,2,3]thiadiazolo[5,4-b]pyridine;

5-[(3*S*,4*R*)-3-fluoro-1-[(*R*)-2-hydroxy-2-(6-methoxyquinolin-4-yl)-ethyl]piperidin-4-ylamino}methyl]- benzo[1,2,3]thiadiazole and 5-[(3*R*,4*S*)-3-fluoro-1-[(*R*)-2-hydroxy-2-(6-methoxyquinolin-4-yl)-ethyl]piperidin-4-ylamino}methyl]- benzo[1,2,3]thiadiazole; {3-Fluoro-1-[(*R*)-2-hydroxy-2-(6-methoxy-[1,5]naphthyridin-4-yl)-ethyl]-piperidin-4-yl}-[1,2,3]thiadiazolo[5,4-*b*]pyridin-6-ylmethyl-amine Diastereoisomer 1; or a pharmaceutically acceptable derivative thereof.

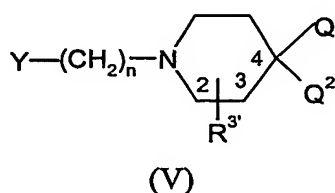
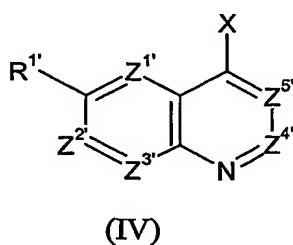
10. A method of treatment of bacterial infections in mammals, particularly in man, which method comprises the administration to a mammal in need of such treatment an effective amount of a compound according to claim 1.

11. The use of a compound according to claim 1, in the manufacture of a medicament for use in the treatment of bacterial infections in mammals.

12. A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier.

13. A process for preparing compounds according to claim 1, which process comprises:

reacting a compound of formula (IV) with a compound of formula (V):



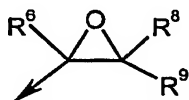
wherein *n* is as defined in formula (I); *Z*^{1'}, *Z*^{2'}, *Z*^{3'}, *Z*^{4'}, *Z*^{5'}, *R*^{1'} and *R*^{3'} are *Z*¹, *Z*², *Z*³, *Z*⁴, *Z*⁵, *R*¹ and *R*³ as defined in formula (I) or groups convertible thereto; *Q*¹ is *NR*^{2'}*R*^{4'} or a group convertible thereto wherein *R*^{2'} and *R*^{4'} are *R*² and *R*⁴ as defined in formula (I) or groups convertible thereto and *Q*² is H or *R*^{3'} or *Q*¹ and *Q*² together form an optionally protected oxo group; and *X* and *Y* may be the following combinations:

- (i) *X* is A'-COW, *Y* is H and *n* is 0;
- (ii) *X* is CR⁶=CR⁸R⁹, *Y* is H and *n* is 0;
- (iii) *X* is oxirane, *Y* is H and *n* is 0;

- (iv) X is $\text{N}=\text{C}=\text{O}$ and Y is H and n is 0;
 (v) one of X and Y is CO_2R^Y and the other is $\text{CH}_2\text{CO}_2\text{R}^X$;
 (vi) X is CHR^6R^7 and Y is $\text{C}(=\text{O})\text{R}^9$;
 (vii) X is $\text{CR}^7=\text{PR}^Z_3$ and Y is $\text{C}(=\text{O})\text{R}^9$ and $n=1$;
 5 (viii) X is $\text{C}(=\text{O})\text{R}^7$ and Y is $\text{CR}^9=\text{PR}^Z_3$ and $n=1$;
 (ix) Y is COW and X is $\text{NHR}^{11'}$ or $\text{NR}^{11'}\text{COW}$ and $n=0$ or 1 or when $n=1$ X is COW and Y is $\text{NHR}^{11'}$ or $\text{NR}^{11'}\text{COW}$;
 (x) X is $\text{C}(=\text{O})\text{R}^6$ and Y is $\text{NHR}^{11'}$ or X is $\text{NHR}^{11'}$ and Y is $\text{C}(=\text{O})\text{R}^8$ and $n=1$;
 (xi) X is $\text{NHR}^{11'}$ and Y is $\text{CR}^8\text{R}^9\text{W}$ and $n=1$;
 10 (xii) X is $\text{CR}^6\text{R}^7\text{W}$ and Y is $\text{NHR}^{11'}$ or OH and $n=1$;
 (xiii) X is $\text{CR}^6\text{R}^7\text{SO}_2\text{W}$ and Y is H and $n=0$;
 (xiv) X is W or OH and Y is CH_2OH and $n=1$;
 (xv) X is $\text{NHR}^{11'}$ and Y is SO_2W or X is $\text{NR}^{11'}\text{SO}_2\text{W}$ and Y is H, and $n=0$;
 (xvi) X is $\text{NR}^{11'}\text{COCH}_2\text{W}$ or $\text{NR}^{11'}\text{SO}_2\text{CH}_2\text{W}$ and Y is H and $n=0$;
 15 (xvii) X is W and Y is $\text{CONHR}^{11'}$;

in which W is a leaving group, e.g. halo or imidazolyl; R^X and R^Y are (C_{1-6}) alkyl; R^Z is aryl or (C_{1-6}) alkyl; A' and $\text{NR}^{11'}$ are A and NR^{11} as defined in formula (I), or groups convertible thereto; and oxirane is:

20



- wherein R^6 , R^8 and R^9 are as defined in formula (I);
 and thereafter optionally or as necessary converting Q^1 and Q^2 to $\text{NR}^{2'}\text{R}^{4'}$; converting A' ,
 Z^1 , Z^2 , Z^3 , Z^4 , Z^5 , R^1 , R^2 , R^3 , R^4 and $\text{NR}^{11'}$ to A, Z^1 , Z^2 , Z^3 , Z^4 , Z^5 , R^1 , R^2 , R^3 ,
 25 R^4 and $\text{NR}^{11'}$; converting A-B to other A-B, interconverting R^1 , R^2 , R^3 and/or R^4 ,
 and/or forming a pharmaceutically acceptable derivative thereof.